CLAIMS

1. The use of a 5-HT2C receptor antagonist in the manufacture of a medicament for the treatment of negative symptoms of and/or cognitive dysfunction in schizophrenia, refractory schizophrenia, suicidality or mild cognitive impairment, with the proviso that:
(a) for the treatment of negative symptoms of and/or cognitive dysfunction in schizophrenia or refractory schizophrenia, the 5-HT2C receptor antagonist is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone;
(b) for the indications cognitive dysfunction in schizophrenia or mild cognitive impairment, the 5-HT2C receptor antagonist is other than (1R,2S,4R)-(-)-2-phenyl-2-(dimethylaminoethoxy)-1,7,7-trimethyl-bicyclo[2.2.1]heptane, (1R,2S,4R)-(-)-2-phenyl-2-(methylaminoethoxy)-1,7,7-trimethyl-bicyclo[2.2.1]heptane and pharmaceutically acceptable acid addition salts thereof; and
(c) for the treatment of schizophrenic suicidality, the 5-HT2C receptor antagonist is other than clozapine.

2. The use of a 5-HT2C receptor antagonist in the manufacture of a medicament for the treatment of negative symptoms of schizophrenia, with the proviso that the antagonist is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone.

3. The use of a 5-HT2C receptor antagonist in the manufacture of a medicament for the treatment of cognitive dysfunction in schizophrenia, with the proviso that the antagonist is other than ritanserin, clozapine, fluperlapine,

loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine, deramciclane, N-desmethylderamiclane or ziprasidone.

4. The use of a 5-HT2C receptor antagonist in the manufacture of a medicament for the treatment of refractory schizophrenia, with the proviso that the antagonist is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone.

5. The use of a 5-HT2C receptor antagonist in the manufacture of a medicament for the treatment of suicidality, with the proviso that, when the suicidality is in a schizophrenic patient, the 5-HT2C receptor antagonist is other than clozapine.

6. The use of claim 5, wherein the suicidality is in a schizophrenic patient.

7. The use of a 5-HT2C receptor antagonist in the manufacture of a medicament for the treatment of mild cognitive impairment with the proviso that the antagonist is other than deramciclane or N-desmethylderamciclane.

8. The use of any one of claims 1 to 7 wherein the 5-HT2C receptor antagonist is as described in one of WO 97/16429, WO 97/44334, US 05010078, EP 161,218, EP 401,707, EP 526,434, DE 02834114, EP 210,893, US 03580916, US 05043341, EP 620,222, EP 208,235, EP 437,790, DE 02614406, US 04338317, EP 271,013, EP 110,435, EP 398,326, WO 92/05170, WO 95/01976, WO 96/23783, WO 98/04289, WO 97/48700, WO 00/48602, WO 00/26186, WO 99/58490, WO 99/52517, WO 99/51237, WO 99/46245, WO 99/43319, WO 99/33841, WO 99/33840, WO 99/25356, WO 99/09017, WO 99/03833, WO 99/00119, WO 98/56367, WO 98/52943, WO 98/50358, WO

98/50346, WO 98/50343, WO 98/41527, WO 98/38165, WO 98/30561, WO 98/30546, WO 98/24785, WO 98/21958, WO 98/04261, WO 97/48699, WO 97/41858, WO 97/39001, WO 97/37989, WO 97/20845, WO 97/12880, WO 97/08167, WO 97/06155, WO 97/00872, WO 96/39382, WO 96/30366, WO 96/24351, WO 96/23769, WO 96/18629, WO 96/14320, WO 96/11930, WO 96/11929, WO 96/02537, WO 95/29177, WO 95/25731, WO 95/24194, WO 95/21844, WO 95/18117, WO 95/12591, WO9 94/22871, WO 94/18958, WO 94/18182, WO 94/18170, WO 94/14801, WO 94/04533, WO 94/02462, WO 93/18028, WO 93/18026, WO 93/16081, WO 93/16051, WO 93/14758, WO 93/12790, WO 92/15302, WO 92/10192, WO 91/18602, WO 01/68585, WO 01/68067, WO 01/52855, WO 01/38329, WO 01/26621, WO 01/25229, WO 01/19371, WO 00/76984, WO 00/68181, WO 00/63185, WO 00/62782, WO 00/61129, WO 00/61128, WO 00/37068, WO 00/06165, US 06143325, US 05854248, US 05739336, US 05693645, US 05674875, US 05498618, US 05371093, US 05266571, US 05116852, US 05106855, US 05030656, US 05013735, US 04985352, US 04914107, US 04914100, US 04906639, US 04902691, US 04891376, US 04847261, JP 13220375, JP 12204040, JP 11171865, JP 11080155, JP 10316634, JP 10077271, JP 09040646, JP 08053416, JP 08040999, JP 07228573, JP 07179337, JO 00158067, GB 02303303, GB 02301774, EP 01118610, EP 1070716, EP 01052245, EP 01000944, EP 00905136, EP 00797995, EP 00797994, EP 00769297, EP 00749971, EP 00749967, EP 00718299, EP 00700905, EP 00686393, EP 00682015, EP 0661266, EP 00657426, EP 006554440, EP 00613898, EP 00596449, EP 00559569, EP 00545120, EP 00522226, EP 00511074, EP 00511073, EP 00493687, EP 00484988, EP 00465398, EP 00452074, EP 00389352, EP 00388081, EP 00384228, EP 00379308, EP 00378468, EP 00375297, EP 00374042, EP 00373998, EP 00363963, EP 00354030, EP 00337136, EP 00332528, EP 00320983, EP 00218433 and EP 00145494.

9. The use of any one of claims 1 to 7 in which the 5-HT2C receptor antagonist is AHR-16303B (AH Robins Co. Inc), AP-792 and AT-1015 (Ajinomoto Co. Inc.), BMS-181102 (Bristol Myers Squibb), CV-5197 (Takeda Chemical Industries Ltd), dotarizine (Ferrer Internacional SA), E-2101 (Eisai Co Ltd), eltoprazine (Solvay SA), emopamil (Knoll AG), HT-90B (Chugai Pharmaceutical Co Ltd), ICI-169369 and ICI-170809 (Zeneca Group plc), LU-26042 and LU-29066 (H Lundbeck A/S), NPC-18166 (Scios Inc), Org-38457 (NV Organon), pelanserin (Cinvestav), perbufylline (Siegfried Group), SB-206553 and SB-242084 (SmithKline Beecham), SR-46615A (Sanofi Recherche SA), SUN-9221 (Suntory Ltd) tropoxin (Russian Academy Medical Science) or YM-992 (Yamanouchi Pharmaceutical Co Ltd).

10. The use of any one of claims 1 to 7 in which the 5-HT2C receptor antagonist is Ro-60-0759, RS-102221, SDZ-SER-082, ICI-169369, deramciclane, N-desmethyl-deramciclane, amesergide, sergolexole, CGS-18102A or LU-26042.

11. The use of claim 10 in which the 5-HT2C receptor antagonist is deramciclane, N-desmethyl-deramciclane, amesergide, sergolexole, CGS-18102A or LU-26042.

12. The use of any one of claims 5 to 7 wherein the 5-HT2C receptor antagonist is ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone.

13. The use of a compound having a relative 5-HT2C affinity of ≥ 1.80, wherein the relative 5-HT2C affinity is determined according to formula I:

Formula I: $\frac{X}{A} + \frac{X}{B}$

[wherein: X is the affinity of a compound for interaction at the 5-HT2C receptor and A and B are the average affinity values of a compound for interaction at two major sites other than the 5-HT2C receptor] in the manufacture of a medicament for the treatment of negative symptoms of and/or cognitive dysfunction in schizophrenia, refractory schizophrenia, suicidality or mild cognitive impairment, with the proviso that:

(a) for the treatment of negative symptoms of and/or cognitive dysfunction in schizophrenia or refractory schizophrenia, the compound is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone;

(b) for the indications cognitive dysfunction in schizophrenia or mild cognitive impairment, the 5-HT2C receptor antagonist is other than (1R,2S,4R)-(-)-2-phenyl-2-(dimethylaminoethoxy)-1,7,7-trimethyl-bicyclo[2.2.1]heptane, (1R,2S,4R)-(-)-2-phenyl-2-(methylaminoethoxy)-1,7,7-trimethyl-bicyclo[2.2.1]heptane and pharmaceutically acceptable acid addition salts thereof; and

(c) for the treatment of schizophrenic suicidality, the compound is other than clozapine.

14. A method for determining the suitability of a candidate compound for use in the treatment of negative symptoms of and/or cognitive dysfunction in schizophrenia, refractory schizophrenia, suicidality or mild cognitive impairment which comprises:

a) assessing the affinity of the compound at the 5-HT2C receptor;

b) assessing the affinity of the compound at at least two other major sites of said compound interaction;

c) applying the assessed affinities to the following formula:

$$\frac{X}{A} + \frac{X}{B} = Y$$

[wherein: X is the affinity of a compound for interaction at the 5-HT2C receptor and A and B are the average affinity values of a compound for interaction at two major sites other than the 5-HT2C receptor];

and selecting compounds in which $Y \geq 1.80$ as suitable compounds for the treatment of cognitive dysfunction in and/or negative symptoms of schizophrenia, refractory schizophrenia, suicidality or mild cognitive impairment, provided that:

(a) for the treatment of cognitive dysfunction in and/or negative symptoms of schizophrenia or refractory schizophrenia, the compound selected is other than ritanserin, clozapine, fluperlapine, loxapine, ORG-5222, pipamperone, sertindole, olanzapine, zotepine or ziprasidone;

(b) for the indications cognitive dysfunction in schizophrenia or mild cognitive impairment, the 5-HT2C receptor antagonist is other than (1R,2S,4R)-(-)-2-phenyl-2-(dimethylaminoethoxy)-1,7,7-trimethyl-bicyclo[2.2.1]heptane, (1R,2S,4R)-(-)-2-phenyl-2-(methylaminoethoxy)-1,7,7-trimethyl-bicyclo[2.2.1]heptane and pharmaceutically acceptable acid addition salts thereof; and

(c) for the treatment of schizophrenic suicidality, the compound selected is other than clozapine.

15. The use of claim 13 or method of claim 14 in which A and B are different and are independently selected from the group consisting of the 5-HT_{1A}, 5-HT_{2A}, 5-HT_3, 5-HT_6, 5-HT_7, D_1, D_2-S,

D_2-L, D_3, D_4, D_5 M_1, M_2, M_3, M_4, M_5, mACh, α_1, α_2, H_1 or sigma receptors.

16. The use or method of claim 15 in which A is the value for affinity at the 5-HT2A receptor.

17. The use or method of claim 15 in which B is the value for affinity at the D2 receptor.

18. Products containing a 5-HT2C receptor antagonist and a typical antipsychotic as a combined preparation for simultaneous, separate or sequential use in schizophrenia or suicidality therapy, or the treatment of mild cognitive impairment.

19. A product according to claim 18 in which the 5-HT2C receptor antagonist is identified according to the method of any one of claims 14 to 17.

20. A product according to claim 18 in which the 5-HT2C receptor antagonist is as defined in any one of claims 8 to 13.